

AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions and listings of claims in the application.

1. (Currently amended) A method of ~~treatment or prevention~~ ameliorating a symptom of at least one degenerative disorder of muscle, ~~bone, or glucose homeostasis~~ associated with GDF-8, comprising:

- (1) administering an effective amount of a pharmaceutical composition to a mammal, wherein the composition comprises an ActRIIB fusion polypeptide comprising (a) an amino acid sequence that is at least ~~80%~~ 95% identical to amino acids 23 to 138 of SEQ ID NO:3 and is capable of binding to GDF-8, and (b) an Fc portion of an antibody; and
- (2) allowing the composition to inhibit GDF-8 activity, thereby ameliorating a symptom of the degenerative disorder.

2. (Original) The method of claim 1, wherein the mammal is human.

3. (Currently amended) The method of claim 1, wherein the pharmaceutical composition is administered to a mammal in need of ~~treatment or prevention~~ ameliorating a symptom of a disorder chosen from ~~at least one of muscle disorder[,] and neuromuscular disorder, and bone degenerative disorder.~~

4. (Currently amended) The method of claim 1, wherein the pharmaceutical composition is administered to a mammal in need of ~~treatment or prevention~~ ameliorating a symptom of a disorder chosen from at least one of muscular dystrophy, Duchenne's muscular dystrophy, muscle atrophy, ~~organ atrophy, carpal tunnel-~~

~~syndrome congestive obstructive pulmonary disease, sarcopenia, cachexia, and muscle wasting syndrome, and amyotrophic lateral sclerosis.~~

5. (Currently amended) The method of claim 1, wherein the pharmaceutical composition is administered to a mammal in need of ~~treatment or prevention~~ ameliorating a symptom of Duchenne's muscular dystrophy.

6-9. (Canceled)

10. (Original) The method of claim 1, wherein the pharmaceutical composition is administered to a mammal in need for repair of damaged muscle.

11. (Previously presented) The method of claim 10, wherein the damaged muscle is myocardiac muscle or diaphragm.

12. (Previously presented) The method of claim 1, wherein the ActRIIB fusion polypeptide is administered at an effective amount chosen from 1 µg/kg to 20 mg/kg, 1 µg/kg to 10 mg/kg, 1 µg/kg to 1 mg/kg, 10 µg/kg to 1 mg/kg, 10 µg/kg to 100 µg/kg, 100 µg to 1 mg/kg, and 500 µg/kg to 1 mg/kg.

13. (Original) The method of claim 1, wherein the first amino acid sequence of said ActRIIB fusion polypeptide comprises amino acids 23 to 138 of SEQ ID NO:3.

14. (Original) The method of claim 1, wherein the first amino acid sequence of said ActRIIB fusion polypeptide comprises amino acids 19 to 144 of SEQ ID NO:1.

15. (Original) The method of claim 1, wherein the second amino acid sequence of said ActRIIB fusion polypeptide comprises a sequence chosen from (a) the Fc fragment of IgG, (b) the Fc fragment of IgG1, (c) the Fc fragment of IgG4, and (d) amino acids 148 to 378 of SEQ ID NO:3.

16. (Original) The method of claim 1, wherein the sequence of the ActRIIB fusion polypeptide is set out in SEQ ID NO:3.

17. (Original) The method of claim 1, wherein circulatory half-life of the ActRIIB fusion polypeptide exceeds 5 days.

18-22. (Canceled)

23. (Previously presented) The method of claim 1, wherein the fusion protein is encoded by a nucleic acid that hybridizes to the complement of SEQ ID NO:4 under stringent hybridization conditions.

24. (Canceled)

25. (Withdrawn-currently amended) A method of inhibiting GDF-8 activity, comprising:

(1) contacting GDF-8 with a composition, wherein the composition comprises an ActRIIB fusion polypeptide comprising (a) an amino acid sequence that is at least 80% 95% identical to amino acids 23 to 138 of SEQ ID NO:3 and is capable of binding to GDF-8, and (b) an Fc portion of an antibody; and

(2) allowing the composition to inhibit GDF-8 activity.

26. (Withdrawn-currently amended) A method of increasing muscle strength, said method comprising:

(1) administering an effective amount of a pharmaceutical composition to a mammal, wherein the composition comprises an ActRIIB fusion polypeptide comprising (a) an amino acid sequence that is at least 80% 95% identical to amino acids 23 to 138 of SEQ ID NO:3 and is capable of binding to GDF-8, and (b) an Fc portion of an antibody; and

- (2) allowing the composition to inhibit GDF-8 activity,
thereby increasing muscle strength.

27-28. (Canceled)

29. (Currently amended) The method of claim 1, wherein the amino acid sequence is at least 85% 97% identical to amino acids 23 to 138 of SEQ ID NO:3.

30. (Currently amended) The method of claim 1, wherein the amino acid sequence is at least 90% 98% identical to amino acids 23 to 138 of SEQ ID NO:3.

31. (Currently amended) The method of claim 1, wherein the amino acid sequence is at least 95% 99% identical to amino acids 23 to 138 of SEQ ID NO:3.

32. (Previously presented) The method of claim 1, wherein the Fc portion is modified to reduce effector function.

33. (Previously presented) The method of claim 1, wherein the Fc portion is modified to reduce binding to an Fc receptor.

34. (Previously presented) The method of claim 1, wherein the Fc portion is modified to reduce complement activation.

35. (Previously presented) The method of claim 1, wherein the Fc portion is unmodified.

36. (New) The method of claim 1, wherein the pharmaceutical composition is administered to a mammal in need of ameliorating a symptom of muscular dystrophy.

37. (New) The method of claim 1, wherein the pharmaceutical composition is administered to a mammal in need of ameliorating a symptom of Duchenne's muscular dystrophy.

38. (New) The method of claim 1, wherein the pharmaceutical composition is administered to a mammal in need of ameliorating a symptom of muscle atrophy.

39. (New) The method of claim 1, wherein the pharmaceutical composition is administered to a mammal in need of ameliorating a symptom of muscle wasting syndrome.